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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/606,502	06/26/2003	Robert Martienssen	021031-000210US	5208

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EXAMINER

STRZELECKA, TERESA E

ART UNIT

PAPER NUMBER

1637

DATE MAILED: 12/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/606,502	<b>Applicant(s)</b> MARTIENSSEN ET AL.	
	<b>Examiner</b> Teresa E. Strzelecka	<b>Art Unit</b> 1637	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 107-137 is/are pending in the application.  
     4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 107-137 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____.  |

## DETAILED ACTION

### *Election/Restrictions*

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
  - I. Claims 107-133, drawn to a method for determining methylation profile of a cell, tissue or organism the method comprising:
    - a. providing a population of randomly cleaved or sheared DNA fragments from the cell, tissue, or organism;
    - b. reducing the percent of unmethylated fragments of interest to no more than 40% of the original percent in the population or reducing the percent of methylated fragments of interest to no more than 40% of the original percent in the population; and
    - c. quantifying the amount of at least one DNA sequence from step (b) to determine the methylation profile of at least one nucleic acid sequence from the cell, tissue or organism, classified in class 435, subclass 6, for example.
  - II. Claims 134-137, drawn to a solid support displaying a polynucleotide, the polynucleotide hybridizing to a labeled DNA portion, wherein the portion is from a population of randomly cleaved or sheared DNA fragments from the cell, tissue, or organism, classified in class 536, subclass 23.1, for example.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant

Art Unit: 1637

case the method of Group I can be practiced with oligonucleotide probes in a homogeneous assay, rather than with the support of Group II.

Searching the inventions of Groups I and II together would impose serious search burden. The inventions of Groups I and II have a separate status in the art as shown by their different classifications. Moreover, in the instant case, the search for the polynucleotides and the method of determining a methylation are not coextensive. Group II encompasses molecules which are claimed in terms of being derived from a population of randomly cleaved or sheared DNA fragments. In contrast, the search for group I would require a text search for the method of determining the methylation status using any way to quantitate methylated or unmethylated DNA sequences. Prior art which teaches a polynucleotides of Group II would not necessarily be applicable to the method of Group I. Moreover, even if the polynucleotide product were known, the method of using the product may be novel and unobvious in view of the preamble or active steps.

3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

4. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments

Art Unit: 1637

submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

5. This application contains claims directed to the following patentably distinct species of the claimed invention:

Species of step (b) of claim 107

A) reducing the percent of unmethylated fragments to no more than 40% of the original population (claim 108),

Art Unit: 1637

B) reducing the percent of methylated fragments to no more than 40% of the original population (claim 109),

C) step (b) comprises depleting methylated or unmethylated DNA and depleting step comprises digesting the cleaved or sheared DNA with methylation-sensitive or methylation-dependent restriction enzyme (claims 112-114),

D) the sheared DNA fragments comprise a first and second portion, depleting of methylated or unmethylated DNA is performed for a second portion using methylation-sensitive or methylation-dependent restriction enzyme (claims 112, 115-117, 129, 132, 133),

E) methylated DNA is depleted from sheared DNA (claims 112, 118),

F) unmethylated DNA is depleted from sheared DNA (claims 112, 119).

Species of quantifying step

A) quantifying step comprises quantitative amplification (claim 110),

B) quantification step comprises hybridizing the DNA reduced of methylated or unmethylated DNA to a nucleic acid linked to a solid support (claims 120, 121).

Species of comparison of methylation profiles

A) methylation profile of a nucleic acid is compared with a transcription profile of the nucleic acid (claims 123, 124),

B) methylation profile of a nucleic acid is compared with a chromatin packaging state profile of the nucleic acid (claim 125),

C) methylation profile of a specimen of a bacterial pathogen is compared with a reference strain of the pathogen (claim 126),

D) methylation profile of a nucleic acid is compared with the copy number of the nucleic acid (claims 127, 128),

Art Unit: 1637

E) methylation profiles of a first and second DNA samples are compared, and the first portion from the first sample, the second portion from the first sample, the first portion from the second sample and the second portion from the second sample are each labeled and hybridized to a nucleic acid, wherein the ratio of the hybridization of the first portions provides a CGH profile and the ratio of the hybridization of the first and second portions for each sample provides a methylation profile for each sample (claims 129, 130),

F) methylation profiles of a first and second DNA samples are compared, and two portions are labeled and hybridized to a nucleic acid, wherein the two portions are either the first portion from the first sample and the second portion from the first; the second portion from the first sample and the first portion from the second sample; the first portion from the second sample and the second portion from the second sample; or the second portion of the second sample and the first portion of the first sample (claims 129, 131).

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 107 is generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Art Unit: 1637

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

6. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E. Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Art Unit: 1637

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

December 20, 2005

**TERESA STRZELECKA**  
**PATENT EXAMINER**

*Teresa Strzelecka*